

Medical Genetics Summaries (MGS): Pharmacogenetics beyond the drug label

Malheiro A.J., Dean L.C., Hoepfner M.A., and Kattman B.L.

Medical Genetics Summaries (MGS)

Unites the latest drug and gene information with dosing recommendations from the FDA, and other professional societies:

18 have recommendations from the Dutch Pharmacogenetics Working Group (DWPG)

14 have recommendations from the Clinical Pharmacogenetics Implementation Consortium (CPIC)

3 have recommendations from the American Society of Clinical Oncology (ASCO)

Other guideline sources include: Canadian Pharmacogenomics Network for Drug Safety (CPNDS), French National Network of Pharmacogenetics (RNPGx), American College of Rheumatology (ACR), and more.

MGS simplifies the implementation of precision medicine

- Explains the influence of genetic variant(s) on drug action and metabolism
- Links to relevant tests in the NIH Genetic Testing Registry (<https://www.ncbi.nlm.nih.gov/gtr/>)
- Standardized for quick reference, up-to-date, centralized source of pharmacogenetics information

NIH Genetic Testing Registry (GTR)

The GTR comprises ~60,000 orderable, genetic tests, which have been voluntarily submitted by genetic testing labs from across the world.

Of these tests, 407 are pharmacogenetic tests, testing for at least one drug response, with some tests analyzing a panel of genetic variants, accounting for over 100 drug responses.

The FDA lists 170 therapeutic products with pharmacogenetic information in the drug labelling. Approximately 99 of these drugs have tests in GTR.

MGS brings together pharmacogenetic dosing guidelines and summarizes the evidence

Capecitabine Therapy and *DPYD* Genotype

Dean L.

[Publication Details](#)

Estimated reading time: 10 minutes

Introduction

Capecitabine is a chemotherapy agent that belongs to the drug class of fluoropyrimidines. It is widely used in the treatment of colon cancer, metastatic colorectal cancer, and metastatic breast cancer. Capecitabine is a prodrug that is enzymatically converted to its active form, fluorouracil, which acts as an antimetabolite to slow tumor growth.

The *DPYD* gene encodes dihydropyrimidine dehydrogenase (DPD), an enzyme that catalyzes the rate-limiting step in fluorouracil metabolism. Individuals who are carriers of non-functional *DPYD* variants, such as *DPYD**2A, may not be able to metabolize capecitabine at normal rates, and are at risk of potentially life-threatening capecitabine toxicity, such as bone marrow suppression and neurotoxicity. The prevalence of DPD deficiency in Caucasians is approximately 3%-5%.

The FDA-approved drug label for capecitabine states that no capecitabine dose has been proven safe in patients with absent DPD activity, and that there is insufficient data to recommend a specific dose in patients with partial DPD activity as measured by any specific test (1).

The Clinical Pharmacogenetics Implementation Consortium (CPIC) has published dosing recommendations for fluoropyrimidines (capecitabine, fluorouracil, and tegafur) based on *DPYD* genotype (2) (Table 1). CPIC recommends using an alternative drug for patients who are “poor metabolizers”. These individuals carry two copies of non-functional *DPYD* variants and

Not at your computer? Each summary can be viewed in PubReader (shown above) for easy reading on small screens, or a summary or the whole book can be downloaded in PDF format.

MGS and GTR are free, easy to use, and ready to help you optimize your care today

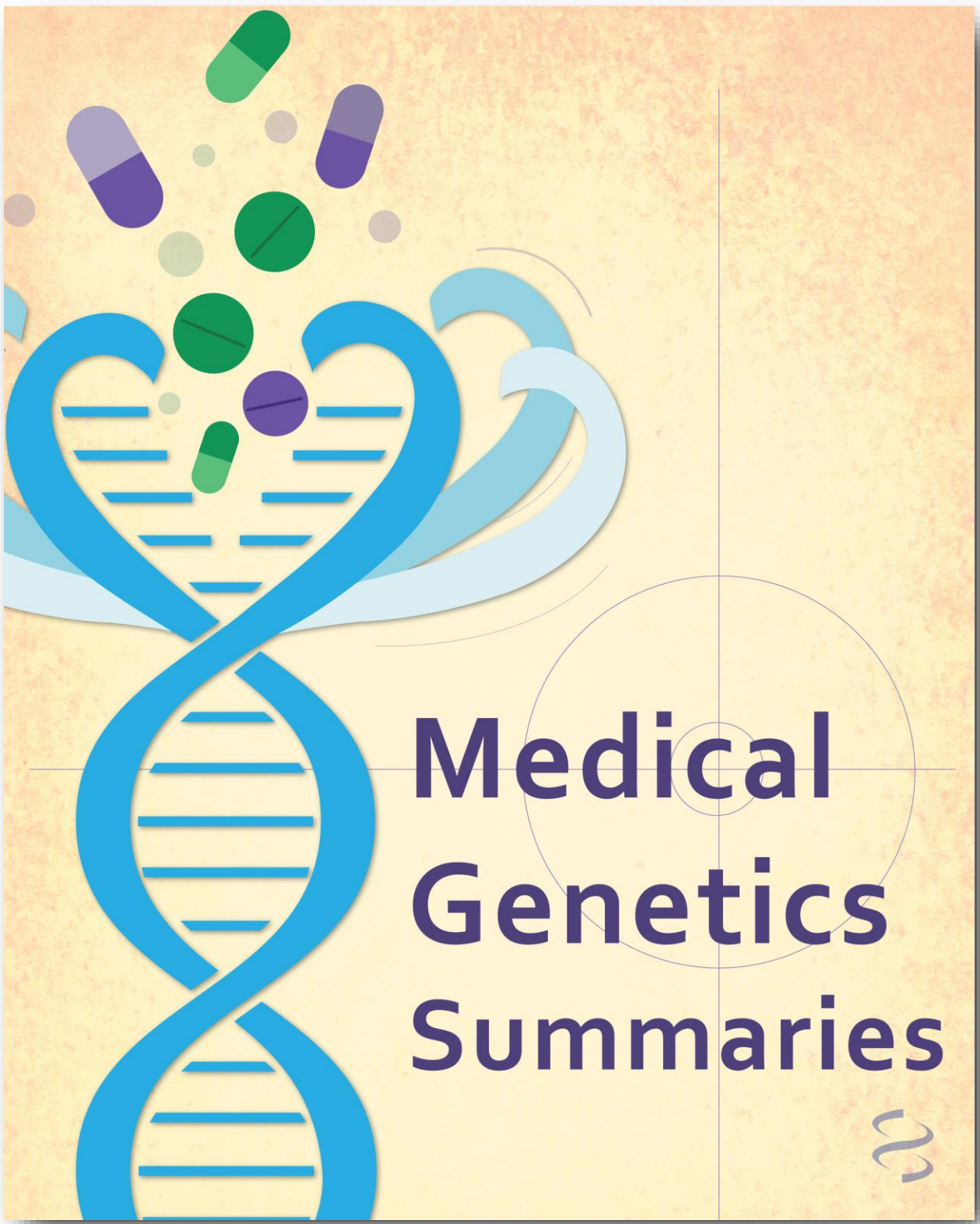
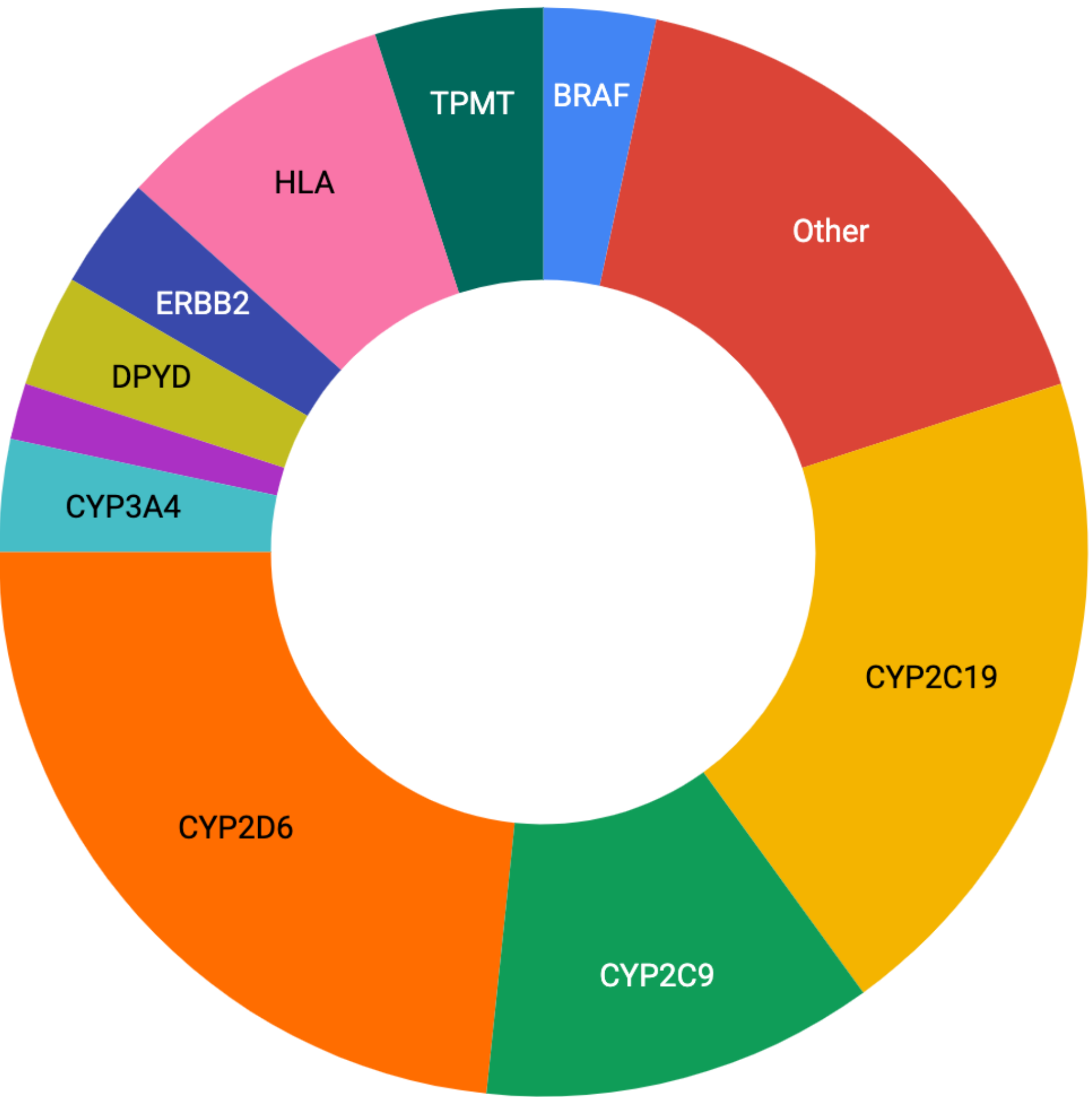
Genes discussed in MGS

CYP2D6 (23%) is the most common gene

Followed by CYP2C19 (20%) and CYP2C9 (12%)

“Other” includes the following genes

- G6PD*
- INFL3*
- IFNL4*
- MT-RNR1*
- NRAS*
- UGT1A1*
- VKORC1*



Medical Genetics Summaries is:

- Indexed in PubMed
- Displayed in GTR and MedGen and ready to display in your EHR – contact us
- Available as full-text online and as PDF from NCBI Bookshelf: <http://go.usa.gov/xVEhN>

MGS in numbers

- 6 editors
- 48 drug summaries
- 100 expert reviewers from clinical, research and laboratory settings

The MGS top 5

The most popular summaries are about the following drugs:

- Codeine
- Warfarin
- Clopidogrel
- Azathioprine
- Allopurinol



Acknowledgements

This research was supported by the Intramural Research Program of the NIH, National Library of Medicine.

Contact us

Visit us in booth #214

Email: mgs@ncbi.nlm.nih.gov

